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The NICHD Connection

January 2022

INSIDE THIS ISSUE

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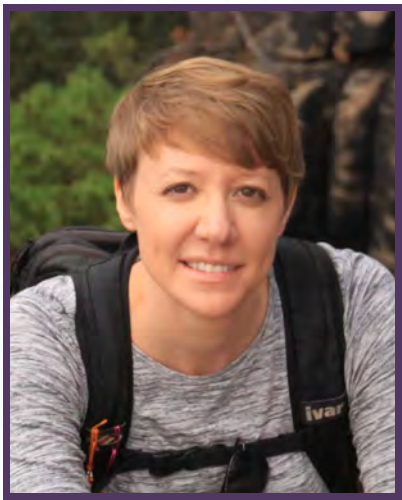
The 2021 NICHD DIR and DIPHR Scientific Retreat at a Glance

By Elliot Murphy, PhD

The lineup of investigators and trainees during the fully virtual NICHD DIR & DIPHR Scientific Retreat on November 5, 2021, showcases the institute's commitment to its central vision: ***Healthy Pregnancies. Healthy Children***. ***Healthy and Optimal Lives.*** Even under the weight of a global pandemic, the NICHD intramural program has generated impactful and exciting scientific research within a diverse set of topics. Indeed, a broad spectrum of ideas and expertise enables NICHD to foster the breadth of research needed to tackle the primary themes of the **NICHD Strategic Plan**. The essence of each theme (described within) was clearly on display at the retreat.

Beginning with the retreat's keynote presentation by **Katherine Rogers, PhD**, principal investigator in the Unit on Developmental Signaling, several speakers touched upon the objectives laid out in the Strategic Plan's first theme: ***Understanding the Molecular, Cellular, and Structural Basis of Development***.

Dr. Rogers, who started her lab at NICHD in July 2021, develops tools and assays to better understand the formation of gene expression patterns in embryos. Her approach activates signaling pathways in zebrafish embryos in response to specific wavelengths of light, in a process known as molecular optogenetics. By controlling the amplitude of the light source, Dr. Rogers observes how varying levels of signaling differentially regulate gene expression.[1] She can also probe the combinatorial effects of multiple signaling pathways by activating individual pathways with different wavelengths of light. These optogenetic tools lay the groundwork for many exciting new studies into the nature of embryonic gene expression and cellular differentiation.



Katherine Rogers, PhD

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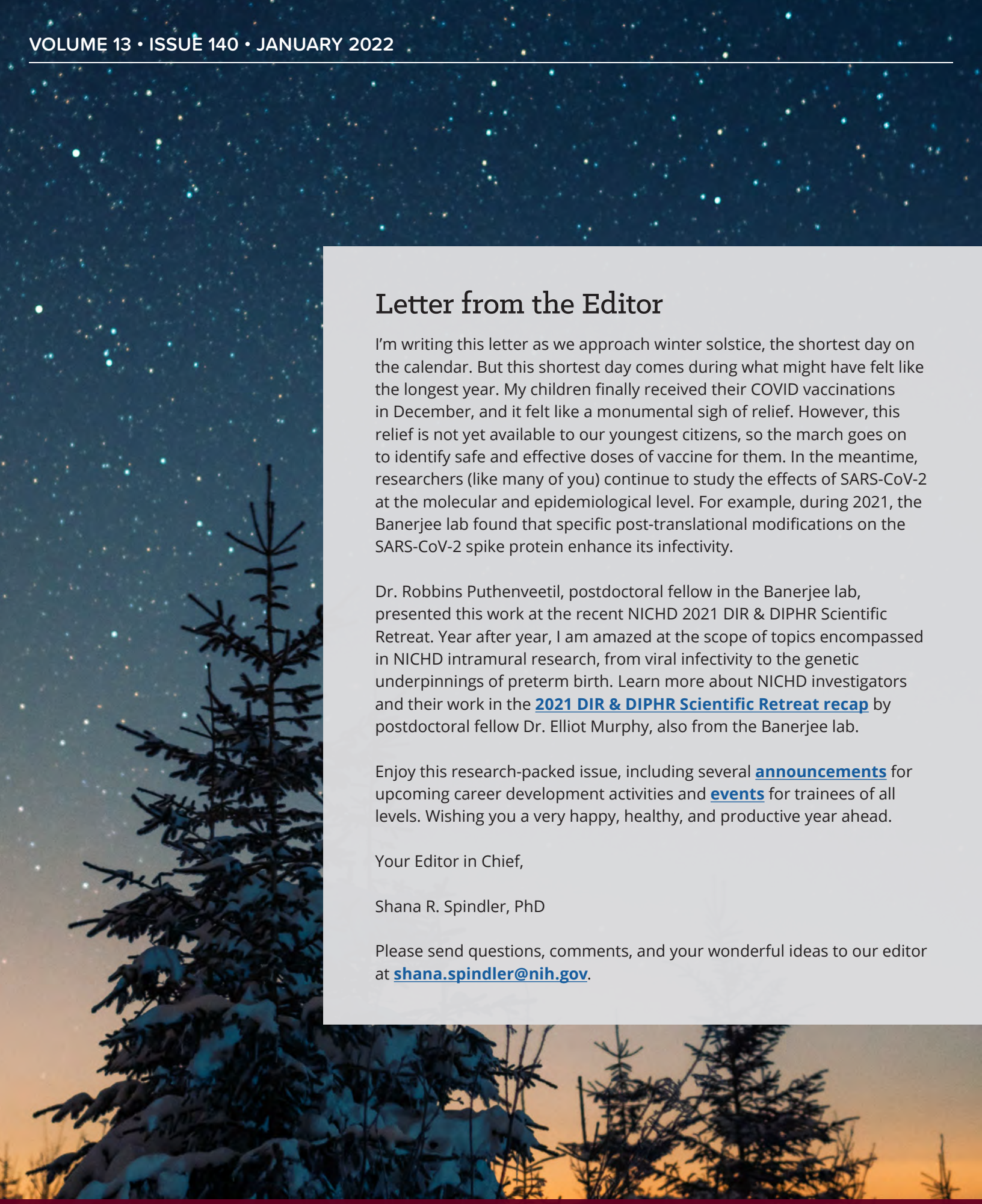


Letter from the Editor

I'm writing this letter as we approach winter solstice, the shortest day on the calendar. But this shortest day comes during what might have felt like the longest year. My children finally received their COVID vaccinations in December, and it felt like a monumental sigh of relief. However, this relief is not yet available to our youngest citizens, so the march goes on to identify safe and effective doses of vaccine for them. In the meantime, researchers (like many of you) continue to study the effects of SARS-CoV-2 at the molecular and epidemiological level. For example, during 2021, the Banerjee lab found that specific post-translational modifications on the SARS-CoV-2 spike protein enhance its infectivity.

Dr. Robbins Puthenveetil, postdoctoral fellow in the Banerjee lab, presented this work at the recent NICHD 2021 DIR & DIPHR Scientific Retreat. Year after year, I am amazed at the scope of topics encompassed in NICHD intramural research, from viral infectivity to the genetic underpinnings of preterm birth. Learn more about NICHD investigators and their work in the **2021 DIR & DIPHR Scientific Retreat recap** by postdoctoral fellow Dr. Elliot Murphy, also from the Banerjee lab.

Enjoy this research-packed issue, including several **announcements** for upcoming career development activities and **events** for trainees of all levels. Wishing you a very happy, healthy, and productive year ahead.

Your Editor in Chief,

Shana R. Spindler, PhD

Please send questions, comments, and your wonderful ideas to our editor at **shana.spindler@nih.gov**.

The 2021 NICHD DIR and DIPHR Scientific Retreat at a Glance

(continued from page 1)

Ramesh Chittajallu, PhD

Like Dr. Rogers, many NICHD researchers rely on animal models to understand the molecular and cellular basis of development, but researchers must also recognize the limitations of these models. **Ramesh Chittajallu, PhD**, a staff scientist from the McBain laboratory, seeks to understand whether the inhibitory neurons in mice, an animal model commonly used in neurobiological studies, function similarly to those in humans. Functional analyses show that a specific interneuron subtype in mouse and human fire at similar frequencies and have largely equivalent action potential waveforms, but how they behave following specific types of stimulation differs significantly between the two. Dr. Chittajallu emphasizes that this divergence—and the implications they have on using mouse models for neurological diseases—warrant further study.

Sometimes, the best place to probe for answers to clinically relevant questions is the human genome itself. **Suvo Chatterjee, PhD**, a postdoctoral fellow from the Tekola-Ayele lab, uses genome wide association studies (GWAS) to identify genetic loci associated with preterm birth.

Suvo Chatterjee, PhD

This genetic analysis relies on data from the **NICHD Fetal Growth Study**[2], a group of over 2,000 low-risk, ethnically diverse pregnant women from 12 US clinical sites. Dr. Chatterjee found that preterm birth is associated with eight loci in seven genes. In comparison to previous studies, only one of these loci was replicated among African and Hispanic women, whereas three loci were replicated among European women. These results emphasize the need for continued studies focusing on more diverse populations to generate reproducible and reliable data.

The second theme emphasized in the NICHD Strategic Plan advocates for the ***Promotion of Gynecologic, Andrologic, and Reproductive Health***. Several presentation topics touched on this theme, including female fertility following childhood cancer treatments, the influence of fibroids on newborn body measurements and preterm birth, and the effect of recreational activity on placental DNA methylation.

(continued on page 4)

The 2021 NICHD DIR and DIPHR Scientific Retreat at a Glance

(continued from page 3)

With increasing childhood cancer survival rates, about 400,000 cancer survivors reside in the United States[3], but for many of them, radiation treatments or chemotherapy have damaged their reproductive organs. **Jacqueline Maher, MD**, staff clinician in the Gomez-Lobo lab, presented her work on understanding how cancer treatments during childhood and adolescence affect female fertility. She found that a childhood cancer survivor's anti-Mullerian hormone (AMH) level—a marker of ovarian reserve—was associated with infertility risk, and the patient's cancer type and treatment(s) gonadotoxicity level based on the Oncofertility Pediatric Initiative Network risk stratification system[4] predicted their AMH levels. Surprisingly, Dr. Maher also observed that almost 10 percent of the women in the high-risk group for infertility did eventually become pregnant. These findings, based on a meta-analysis of 14 studies including over 600 patients' individual data, emphasizes the complex nature of post-treatment counseling.

Jacqueline Maher, MD

Another presenter to showcase research on gynecological health was **Susanna Mitro, PhD**, postdoctoral fellow from the Grantz laboratory, whose work reveals that fibroids (benign tumors that grow in the uterus) lead to larger neonatal head and arm circumference as well as a greater frequency of preterm birth. For her statistical analysis, Dr. Mitro used patient data from the **NICHD Fetal Growth Study**[2] to investigate associations between the visualization of fibroids in ultrasounds taken at multiple points throughout the pregnancy and neonatal metrics. She categorized patients based on number of fibroids and fibroid size. According to Dr. Mitro's analysis, the increased head circumference associated with fibroid observation appears to be unrelated to the risk of preterm birth.

Susanna Mitro, PhD

Taking an epigenetic approach, **Sifang (Kathy) Zhao, PhD**, postdoctoral fellow who has worked with Drs. Yeung and Zhang in the Epidemiology Branch, presented her recent findings from an epigenome-wide association study on the correlation between maternal physical activity and placental DNA methylation. Using

(continued on page 5)

Sifang (Kathy) Zhao, PhD

The 2021 NICHD DIR and DIPHR Scientific Retreat at a Glance

(continued from page 4)

data from the **NICHD Fetal Growth Study**[2], she examined how the timing of physical activity relative to pregnancy affects epigenetic modification in the placenta. Using a questionnaire offered six times throughout pregnancy to a racially diverse population of pregnant women, Dr. Zhao found that physical activity associated with placental DNA methylation, which varied based on the timing of the physical activity. The largest change occurred at a site within *TIMP2*, which encodes a protein involved in vasodilation, placentation, and uterine expansion during pregnancy. The finding suggests that lifestyle habits during pregnancy might influence the placenta through epigenetic modifications, a potential mechanism driving the intergenerational influence of physical activity.

Ruijin Lu, PhD

Like Dr. Zhao, multiple presenters at the retreat discussed studies with implications for improving pregnancy outcomes and maximizing the health of women and their children. This perfectly ties in with the third theme communicated in the Strategic Plan: ***Setting the Foundation for Healthy Pregnancies and Lifelong Wellness***.

Ruijin Lu, PhD, postdoctoral fellow from the Chen lab, seeks to understand how neonatal outcomes, such as birthweight and birth length, associate with longitudinal lipid profiles from patient blood samples. In her presentation, Dr. Lu focused on the use of statistical analysis to identify specific lipid groups that most relate to neonatal outcomes. She presented her ongoing efforts to develop an algorithm that uses data that is longitudinal, high-dimensional (simultaneously analyzing more than 300 metabolites) and compositional (reliant on the relative abundance of what's measured). Though this study is still ongoing, Dr. Lu and her colleagues have conducted multiple simulations to test their longitudinal method and have found that their algorithm gained more sparsity and higher accuracy in prediction on both simulated data and real data compared to currently available cross-sectional methods.

Maziar Rahmani, MD, PhD, ABIM

Jumping from computer models to animal models, **Maziar Rahmani, MD, PhD, ABIM**, clinical fellow in the Weinstein lab, uses genome-wide RNA profiling in zebrafish to investigate why diabetic individuals exhibit complications of diabetes many years after blood sugar levels have been brought under control—a phenomenon known as "glycemic memory." Dr. Rahmani temporarily exposed zebrafish to hyperglycemic conditions and then periodically analyzed their liver tissue and liver endothelial cells

(continued on page 6)

The 2021 NICHD DIR and DIPHR Scientific Retreat at a Glance

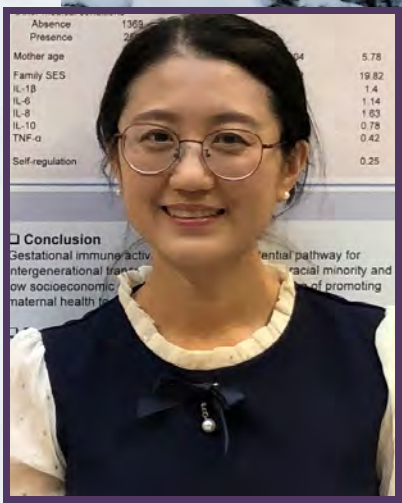
(continued from page 5)

during hyperglycemic and normoglycemic states to identify signaling pathways associated with glycemic memory. He discovered changes in multiple circadian clock genes in vascular endothelial cells. Dr. Rahmani believes his work has implications for understanding the pathogenesis of diabetic vasculopathy, a life-threatening condition.

Continuing with the theme of disease and lifelong wellness, **Tushar P. Patel, PhD**, postdoctoral fellow in the Yanovski lab, focuses his efforts on discerning the role of the melanocortin 3 receptor (MC3R) in metabolism and obesity. Specifically, he asked if MC3R signaling regulates hepatic lipid autophagy (the degradation of liver lipid droplets), given that lipogenic genes are upregulated in mice lacking MC3R.[5] Dr. Patel observed an accumulation of light chain 3 (LC3) II, a classical marker for autophagy, upon activation of MC3R but not further increased LC3II activation in MC3R knockout, which instead caused decreased clearance of lipid droplets and excessive accumulation of autophagosomes. Additionally, he found that a loss of MC3R blocked autophagic degradation and interfered with autophagosome formation. Digging deeper, Dr. Patel discovered that MC3R might play a role in nuclear translocation of TFEB, a transcription factor linked to lysosomal biogenesis. Altogether, Dr. Patel's research provides compelling evidence that MC3R is required for autophagosome formation in the liver, which has implications for understanding the molecular underpinnings of obesity.

Tushar P. Patel, PhD

Two talks in particular highlight the fourth theme of the Strategic Plan, which underlines the institute's commitment to ***Improving Child and Adolescent Health and the Transition to Adulthood***. **Jing Yu, PhD**, research fellow in the Gilman lab, examines the effects of adverse childhood experience (ACEs) on premature mortality, and **Morie Ishida, PhD**, postdoctoral fellow in the Bonifacino lab, studies the impact of genetic mutations on neurological disorders in pediatric patients.



Jing Yu, PhD

Dr. Yu wanted to know if adverse childhood experiences (ACEs), such as parental harshness and neglect, mental illness, divorce, crowded housing, and poverty, might contribute to the underlying causes of racial and socioeconomic disparities in premature mortality. Using data from the **National Collaborative Perinatal Project**[6] and the **National Death Index**, she indeed found that children's race and social class linked to their number of ACEs, and a greater number of ACEs correlated with a higher incidence of premature mortality. Dr. Yu speculates that the impact of ACEs on premature mortality could be explained by lasting biological impacts, such as physiological dysregulation of stress leading to chronic illness later in life, as well as factors that undermine healthy behavioral development.

(continued on page 7)

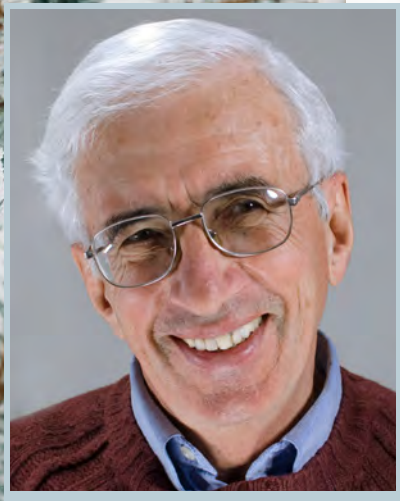
The 2021 NICHD DIR and DIPHR Scientific Retreat at a Glance

(continued from page 6)

Morie Ishida, PhD

Dr. Yu was immediately followed by Dr. Ishida, who investigates the impact of *ARF1* gene mutations on neurological disorders in pediatric patients. The ARF1 protein is a small GTPase that regulates retro- and anterograde sorting and helps maintain the structure of the Golgi apparatus. To understand how the *ARF1* mutations observed in pediatric patients contribute to individual neurological disorders, Dr. Ishida compared the effect of these mutations with those of known constitutively active and inactive versions of the ARF1 protein. He examined a variety of key functions, including the ability to interact with binding partners and to maintain the structure of the Golgi apparatus. Dr. Ishida found that all patient-derived *ARF1* mutations are likely to be gain of function mutations which are constitutively active. Interestingly, the patient-derived mutation that conferred the highest amount of activity linked to lysosomal abnormalities in fibroblasts taken from that patient.

The remaining retreat presentations transition from human development and reproduction to a focus on our understanding of viral infections and disease. These presentations create a foundation for safe and effective anti-viral treatments for the broader public, linking them to the fifth and final theme of the Strategic Plan, ***Advancing Safe and Effective Therapeutics and Devices for Pregnant and Lactating Women, Children, and People with Disabilities***.



Leonid Margolis, PhD

The first of these talks was delivered by **Leonid Margolis, PhD**, senior investigator of the Section on Intercellular Interactions. Dr. Margolis presented his research into the underlying mechanisms of persistent immune activation, even in the absence of viral replication, within HIV-1 infected tissue. The question posed by this research is important because, even though modern antiretroviral therapies can inhibit viral replication in the human body below detectable levels, inflammation caused by persistent immune activation can lead to many adverse outcomes, such as cardiovascular disease and cancer. To understand the presence of immune activation despite the absence of viral replication, Dr. Margolis' group systematically tested reasonable hypotheses until his group found that immune activation is supported by extracellular vesicles carrying HIV-1 molecules. Dr. Margolis believes that characterization of these extracellular vesicles may create a new target for therapy.

(continued on page 8)

The 2021 NICHD DIR and DIPHR Scientific Retreat at a Glance

(continued from page 7)

SARS-CoV-2, the etiological agent behind the COVID-19 pandemic, is a virus with imminent worldwide importance. **Robbins Puthenveetil, PhD**, a postdoctoral fellow in the Banerjee lab, presented novel findings[7] that a post-translational modification called palmitoylation of the SARS-CoV-2 spike protein enhances its infectivity. Dr. Puthenveetil found that spike protein palmitoylation, which involves the attachment of a fatty acid moiety to a cytosolically exposed cysteine residue, predominantly occurs on a cluster of sites located near the transmembrane domain. He also identified multiple specialized enzyme DHHC-palmitoyltransferases that modify these sites to varying degrees. SARS-CoV-2 infectivity was greatly diminished when Dr. Puthenveetil removed the palmitoylation sites via mutagenesis, emphasizing the importance of this modification in the overall viral life cycle.

Robbins Puthenveetil, PhD

During the closing remarks at the retreat, NICHD Postdoctoral Fellow Representative **Lauren Walling, PhD**, thanked both the attendees and the presenters for making this year's retreat a success. In particular, she described the experience as "a great opportunity to learn about some of the outstanding and diverse research that's going on within our institute." Undoubtably, the capacity to maintain a commitment to the specific set of goals laid out in the NICHD Strategic Plan, while also facilitating impactful research on such a diverse spectrum of topics, is one of the NICHD's greatest assets.

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The Rep Report

By Lauren Walling, PhD

As the current NICHD Basic Sciences Institutes and Centers (IC) Representative, I represent NICHD postdoctoral fellows at the Fellows Committee (FelCom) meeting every month and share the latest news with you here. Do you have a concern or question that you want brought up at the next meeting? Contact me at **lauren.walling@nih.gov**!

The December FelCom meeting was a listening session with the NIH Office of Intramural Training and Education (**OITE**) to give feedback on their programming over the last year. Primarily they wanted to hear what did and didn't work well during the pandemic, to inform how they structure future programming as the NIH transitions to a full return to the workplace. Another listening session was held December 15, but if you were unable to attend and want to share your thoughts, please email Dr. Anna Han, OITE Senior Advisor for Social and Behavioral Sciences (**anna.han@nih.gov**).

The **Service and Outreach Subcommittee** is starting a virtual outreach project with Kings Glen Elementary School in Virginia this January. They will be creating and virtually presenting hands-on experiments and activities for their 4th grade science classes. If you are interested in participating, email Surangi Perera (**pererasn@nih.gov**).

I hope everyone enjoyed the holidays! Happy New Year!

January Announcements

SEEKING IMAGE SUBMISSIONS FOR THE 17TH ANNUAL FELLOWS MEETING

We are beginning our search for the feature image of the 17th Annual NICHD Fellows Meeting.

The winning image will be showcased on the fellows retreat website, on posters, and used as the front cover of the event program. Also, to highlight everyone's imagery, all submissions we receive will be used to produce a collage posted on the 2022 retreat website. You can always view image submissions from previous years at **http://retreat.nichd.nih.gov**.

In addition to image resolution and quality, selection criteria include the relevance to our institute's mission and artistic view of the image. All submissions (at the highest possible resolution) should be sent to Nicki Swan (**jonasnic@mail.nih.gov**) by January 31, 2022, with a brief caption for the image.

NICHD ANNUAL POSTBAC SEMINAR SERIES: PROFESSIONAL DEVELOPMENT AND CAREER EXPLORATION

Our Annual Postbac Seminar Series continues into the new year! Join us (virtually) on Wednesdays, from 1 to 2 p.m. (schedule and details on **page 11**). The intent is to create a comfortable environment within a small group of peers to help postbacs improve their analytical skills as scientists, while expanding their knowledge of biomedical research and its relevance to human health.

Currently there are about 100 postbacs conducting clinical and basic science research in our intramural laboratories. During your one or two years of training here at the NICHD, we want you to have an enriched research experience, while at the same time growing more prepared and excited about your chosen career path.

This series also focuses on professional development:

- Learning how to present your science
- Exploring different career trajectories
- Meeting physicians and scientists from various clinical or research settings
- Preparing for the medical or graduate school application cycle (including interviews!)

Have an idea for a seminar topic? Know somebody who would make a great speaker for the series? We want to hear from you! Email Dr. Erin Walsh (**erin.walsh@nih.gov**) with your thoughts.

(continued on page 11)

January Announcements

(continued from page 10)

NICHD ANNUAL POSTBAC SEMINAR SERIES, CONTINUED

Schedule of Topics
(All sessions take place via Zoom from 1 to 2 p.m. unless otherwise indicated)

January 12	How to Evaluate, Build, and Highlight Transferrable Skills (**Propel Careers**)
January 26	Career Planning Step One: Knowing the End of Your Rainbow (Triesta Fowler, MD)
February 2	The Medical School Search and Application Process (Triesta Fowler, MD)
February 9	LinkedIn: Building a Positive Online Personal Brand (**Propel Careers**)
February 16	The Medical School Personal Statement (Triesta Fowler, MD)
To Be Announced	Meet the Scientist: Clinical Research
To Be Announced	Meet the Scientist: Basic Science Research
To Be Announced	The Graduate School Search and Application Process (Erin Walsh, PhD)
To Be Announced	The Graduate School Personal Statement (Erin Walsh, PhD)

Stay-tuned for the final schedule, which will be announced by email soon.

If you are interested in attending, please email Veronica Harker (**veronica.harker@nih.gov**) to register and let her know which sessions you plan to attend. Zoom links will be distributed a few days prior.

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January Announcements

(continued from page 11)

THREE-MINUTE TALKS (TmT) COMPETITION 2022

Now Seeking Postdoc & Clinical Fellows, Graduate Students & Postbacs

- Learn how to explain your research effectively to a broad scientific audience, in three minutes or less, with one-on-one professional training from public speaking coach Scott Morgan.
- Get the chance to win up to $1,000 for use towards approved training or scientific conference participation.
- Visit the **NICHD TmT Program website** for more details: up to 10 DIR fellows (postbac, predoctoral, postdoctoral, visiting and clinical) are invited to compete for these science communication honors.

2022 TmT Program Timeline and Details

Monday, February 7	**Deadline to Enter** » To enter, complete the **2022 Submission Form** » The submission form, competition rules and judging criteria are available at the **NICHD TmT Webpage**
Friday, February 11	**Three-Minute Talk Training/Introductory Workshop** » Tips on scientific storytelling with only one slide » Speaking in plain language while addressing the human health relevance for your research » Creating effective visual aids
March, April, May Dates TBD	**Individual Coaching/Practice Sessions** » Meet one-on-one with public speaking coach Scott Morgan » Practice your talk and obtain feedback on oral presentation skills and speech development
June, Date TBD	**NICHD TmT Competition** » Top three will each be awarded $500 for approved training/travel » Finalist (Top Score) will be chosen to advance to the NIH-wide competition
June, Date TBD	**NIH TmT Competition** » NICHD finalist has a chance at additional $500 award if their score is within the top three overall (With NICHD, NHGRI, NIDCR, NIDCD, NIAMS, NEI, NIDDK, NIDCD, NIAID, NINDS, NLM and NIEHS)

(continued on page 13)

January Announcements

(continued from page 12)

UPCOMING CAREER PLANNING WEBINAR SERIES

Led by Lauren Celano, CEO and Co-founder of Propel Careers

Trainees at all levels are encouraged to attend!

How to Evaluate, Build, and Highlight Transferrable and Career Relevant Skills
Wednesday, January 12, 1–2 p.m.

Lauren Celano will provide insight on how to evaluate the transferable skills that are valued in various scientific careers, highlighting the essential non-scientific skills you can build while performing research, and demonstrating ways to apply these skills in your desired career to achieve your goals. Advice will be provided for various career paths, including research and non-research roles. Lauren will also provide guidance on how to package scientific and non-scientific skills on resumes, cover letters, and during interviews.

Building a Positive Online Personal Brand using LinkedIn
Wednesday, February 9, 1–2 p.m.

For those of you interested in creating or improving your LinkedIn page, this webinar will provide guidance on leveraging this platform for developing your professional online brand. You will dive deep into which parts of a profile to focus on and how to customize your profile to your career area(s) of interest. Lauren Celano will discuss:

- Strategies for highlighting your background and experiences as a compliment to your resume
- How organizations use LinkedIn to identify talent for open positions and which sections are most important
- How to use the job preference features to inform internal and external recruiters about what you're looking for

To register, please email Katherine Lamb (**katherine.lamb@nih.gov**) and indicate which session(s) you plan to attend. The Zoom link will be circulated a few days prior to each.

January Events

WEDNESDAY, JANUARY 12, 1–2 PM

How to Evaluate, Build, and Highlight Transferrable and Career Relevant Skills
Led by Lauren Celano, CEO and co-founder of **Propel Careers**

If you are interested in attending, please email Katherine Lamb (**katherine.lamb@nih.gov**) to register. The Zoom link will be circulated before the session.

WEDNESDAY, JANUARY 26, 1–2 PM

Postbac Seminar Series
Career Planning Step One: Knowing the End of Your Rainbow
Triesta Fowler, MD

Defining a desired career goal is the first step in developing a plan that will help you reach that goal. In this session we will explore the options available for careers in research and medicine. We will then review steps that you can use to develop and execute a career plan. So come prepared to imagine or reimagine what lies for you at the end of your rainbow because the journey will start when you know your destination.

Please email Veronica Harker (**veronica.harker@nih.gov**) to register for this session.

ONGOING EVENTS AROUND CAMPUS

NIH-Wide Office of Intramural Training and Education (OITE) Events
For more information and registration, please visit **Upcoming OITE Events**.

NIH Library Training and Events
For more information and registration, please visit the **NIH Library Calendar**.